REMARKS

The Claims

Claims 82-92 are currently pending in the application. Claim 82 is amended to recite "a transgenic rodent capable of producing human antibodies". Support for the amendment is found at p. 17, lines 28-32 which refers to "transgenic animals capable of producing human antibodies" and references "PCT Application No. WO93/12227". The referenced PCT application is entitled "Transgenic Non-Human Animals Capable of Producing Heterologous Antibodies" and discloses the example of a transgenic rodent (in particular a transgenic mouse) having human Ig genes which confer the ability to produce human antibodies. Applicant maintains that the amended claims does not raise new matter or raise new issues requiring further consideration and/or search. Entry of the amendments is respectfully requested.

Rejection under 35 U.S.C. 112

Claims 82-92 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner argues that the specification fails to provide sufficient guidance "regarding expressing human antibodies directed against osteoprotegerin binding protein in transgenic non-human animals". In addition, the Examiner alleges that the art is unpredictable and extremely complex as evidenced by the disclosures in the Jakobovits and Bruggerman references which were cited during prosecution.

Applicant respectfully traverses the rejection. The Jakobovits and Bruggerman references report the successful production of transgenic mice having human Ig genes which, when injected with an antigen, produced human antibodies to the antigen ("As summarized in Table 2, hybridomas have been isolated from transgenic mice, specific for a variety of cells, proteins, and hapten antigens. Furthermore, immunization with human cells or human CD4 protein can be used to produce human anti-human Mabs", Bruggerman at p. 396). Jakobovits at p. 564 states that transgenic mice can produce human antibodies upon immunization with "model antigens, such as tetanus toxin C, and human antigens such as CD4 and IgE antibody." Clearly, the transgenic mice described in Bruggerman and Jakobovits are capable of producing human antibodies to a variety of antigens.

In the discussion of the references, the Examiner has ignored the positive results reported with transgenic mice and instead emphasizes the "drawbacks regarding human antibody production in mice". One alleged drawback is that Jakobovits "does not address antibodies made against various protein sequences or fragments". In fact, Jakobovits refers to the use of CD4 and IgE antibody, both proteins, to elicit human antibodies in transgenic mice. The other alleged "drawbacks" noted by the Examiner relate primarily to optimizing the human antibody response by transgenic mice (e.g., fully inactivating mouse Ig genes to increase human antibody titer or transferring larger segment of human Ig loci to the mouse germline to increase antibody diversity) and do not alter the conclusion that both Jakobovits and Bruggerman disclose a transgenic animal that is fully capable of producing human antibodies.

One skilled in the art following the Jakobovits and Bruggerman references as examples could apply the teachings therein to the generation of other transgenic animals. There is nothing in the references to suggest otherwise and no reason why one skilled in the art could not do so.

Without acquiescing to the invention and solely to advance prosecution, Applicant has amended Claim 82 to recite "transgenic rodent" and requests that the rejection be withdrawn.

CONCLUSION

Claims 82-92 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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